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ART 34 AMDT

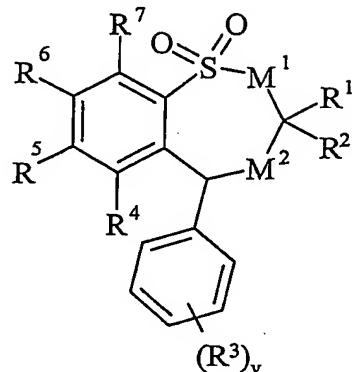
WO 2004/076430

PCT/GB2004/000695

- 57 -

Claims

1. A compound of formula (I):



5

(I)

wherein

M¹ is -CH₂- or -NR²¹-;

M² is -CR²²R²³- or -NR²⁴-; provided that if M¹ is -NR²¹-, M² is -CR²²R²³-;

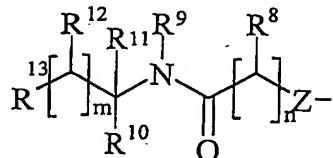
One of R¹ and R² are selected from hydrogen, C₁₋₆alkyl or C₂₋₆alkenyl and the other is
10 selected from C₁₋₆alkyl or C₂₋₆alkenyl;

R³ is selected from halo, nitro, cyano, hydroxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkanoyl, C₁₋₆alkanoyloxy, N-(C₁₋₆alkyl)amino, N,N-(C₁₋₆alkyl)₂amino, C₁₋₆alkanoylamino, N-(C₁₋₆alkyl)carbamoyl, N,N-(C₁₋₆alkyl)₂carbamoyl, C₁₋₆alkylS(O)_a wherein a is 0 to 2, C₁₋₆alkoxycarbonyl,

15 N-(C₁₋₆alkyl)sulphamoyl and N,N-(C₁₋₆alkyl)₂sulphamoyl;

v is 0-5;

one of R⁵ and R⁶ is a group of formula (IA):



(IA)

20 R⁴ and R⁷ and the other of R⁵ and R⁶ are independently selected from hydrogen, halo, nitro, cyano, hydroxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, C₁₋₄alkyl, C₂₋₄alkenyl, C₂₋₄alkynyl, C₁₋₄alkoxy, C₁₋₄alkanoyl, C₁₋₄alkanoyloxy, N-(C₁₋₄alkyl)amino, N,N-(C₁₋₄alkyl)₂amino, C₁₋₄alkanoylamino, N-(C₁₋₄alkyl)carbamoyl,

N,N-(C₁₋₄alkyl)₂carbamoyl, C₁₋₄alkylS(O)_a wherein a is 0 to 2, C₁₋₄alkoxycarbonyl, N-(C₁₋₄alkyl)sulphamoyl and N,N-(C₁₋₄alkyl)₂sulphamoyl; wherein R⁴ and R⁷ and the other of R⁵ and R⁶ may be optionally substituted on carbon by one or more R²⁵;

Z is -O-, -N(R^a)-, -S(O)_b- or -CH(R^a)-; wherein R^a is hydrogen or C₁₋₆alkyl and b is 0-

5 2;

R⁸ is hydrogen, C₁₋₄alkyl, carbocyclyl or heterocyclyl; wherein R⁸ may be optionally substituted on carbon by one or more substituents selected from R²⁶; and wherein if said heterocyclyl contains an -NH- group, that nitrogen may be optionally substituted by a group selected from R²⁷;

10 R⁹ is hydrogen or C₁₋₄alkyl;

R¹⁰ and R¹¹ are independently selected from hydrogen, C₁₋₄alkyl, carbocyclyl or heterocyclyl; or R¹⁰ and R¹¹ together form C₂₋₆alkylene; wherein R¹⁰ and R¹¹ or R¹⁰ and R¹¹ together may be independently optionally substituted on carbon by one or more substituents selected from R²⁸; and wherein if said heterocyclyl contains an -NH- moiety, that nitrogen

15 may be optionally substituted by one or more R²⁹;

R¹² is hydrogen, C₁₋₄alkyl, carbocyclyl or heterocyclyl; wherein R¹² may be optionally substituted on carbon by one or more substituents selected from R³⁰; and wherein if said heterocyclyl contains an -NH- moiety, that nitrogen may be optionally substituted by one or more R³¹;

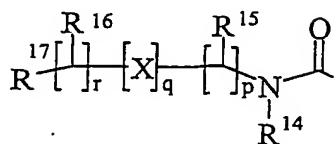
20 R¹³ is hydrogen, halo, nitro, cyano, hydroxy, amino, carbamoyl, mercapto, sulphamoyl, hydroxyaminocarbonyl, C₁₋₁₀alkyl, C₂₋₁₀alkenyl, C₂₋₁₀alkynyl, C₁₋₁₀alkoxy, C₁₋₁₀alkoxycarbonyl, C₁₋₁₀alkanoyl, C₁₋₁₀alkanoyloxy, N-(C₁₋₁₀alkyl)amino, N,N-(C₁₋₁₀alkyl)₂amino, N,N,N-(C₁₋₁₀alkyl)₃ammonio, C₁₋₁₀alkanoylamino, N-(C₁₋₁₀alkyl)carbamoyl, N,N-(C₁₋₁₀alkyl)₂carbamoyl, C₁₋₁₀alkylS(O)_a wherein a is 0 to 2,

25 N-(C₁₋₁₀alkyl)sulphamoyl, N,N-(C₁₋₁₀alkyl)₂sulphamoyl, N-(C₁₋₁₀alkyl)sulphamoylamino, N,N-(C₁₋₁₀alkyl)₂sulphamoylamino, C₁₋₁₀alkoxycarbonylamino, carbocyclyl,

carbocyclylC₁₋₁₀alkyl, heterocyclic group, heterocyclylC₁₋₁₀alkyl, carbocyclyl-(C₁₋₁₀alkylene)_e-R³²-(C₁₋₁₀alkylene)_f or

heterocyclyl-(C₁₋₁₀alkylene)_g-R³³-(C₁₋₁₀alkylene)_h; wherein R¹³ may be optionally substituted

30 on carbon by one or more substituents selected from R³⁶; and wherein if said heterocyclyl contains an -NH- group, that nitrogen may be optionally substituted by a group selected from R³⁷; or R¹³ is a group of formula (IB):



(IB)

wherein:

X is $-\text{N}(\text{R}^{38})-$, $-\text{N}(\text{R}^{38})\text{C}(\text{O})-$, $-\text{O}-$, and $-\text{S}(\text{O})_a-$; wherein a is 0-2 and R^{38} is hydrogen or

5 $\text{C}_{1-4}\text{alkyl}$;

R^{14} is hydrogen or $\text{C}_{1-4}\text{alkyl}$;

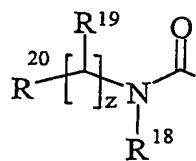
R^{15} and R^{16} are independently selected from hydrogen, halo, nitro, cyano, hydroxy, amino, carbamoyl, mercapto, sulphamoyl, $\text{C}_{1-6}\text{alkyl}$, $\text{C}_{2-6}\text{alkenyl}$, $\text{C}_{2-6}\text{alkynyl}$, $\text{C}_{1-6}\text{alkoxy}$, $\text{C}_{1-6}\text{alkanoyl}$, $\text{C}_{1-6}\text{alkanoyloxy}$, $N-(\text{C}_{1-6}\text{alkyl})\text{amino}$, $N,N-(\text{C}_{1-6}\text{alkyl})_2\text{amino}$,

10 $\text{C}_{1-6}\text{alkanoylamino}$, $N-(\text{C}_{1-6}\text{alkyl})\text{carbamoyl}$, $N,N-(\text{C}_{1-6}\text{alkyl})_2\text{carbamoyl}$, $\text{C}_{1-6}\text{alkylS}(\text{O})_a$ wherein a is 0 to 2, $\text{C}_{1-6}\text{alkoxycarbonyl}$, $N-(\text{C}_{1-6}\text{alkyl})\text{sulphamoyl}$, $N,N-(\text{C}_{1-6}\text{alkyl})_2\text{sulphamoyl}$, carbocyclyl or heterocyclic group; wherein R^{15} and R^{16} may be independently optionally substituted on carbon by one or more substituents selected from R^{41} ; and wherein if said heterocyclyl contains an $-\text{NH}-$ group, that nitrogen may be optionally substituted by a group

15 selected from R^{42} ;

R^{17} is selected from hydrogen, halo, nitro, cyano, hydroxy, amino, carbamoyl, mercapto, sulphamoyl, hydroxyaminocarbonyl, $\text{C}_{1-10}\text{alkyl}$, $\text{C}_{2-10}\text{alkenyl}$, $\text{C}_{2-10}\text{alkynyl}$, $\text{C}_{1-10}\text{alkoxy}$, $\text{C}_{1-10}\text{alkanoyl}$, $\text{C}_{1-10}\text{alkanoyloxy}$, $N-(\text{C}_{1-10}\text{alkyl})\text{amino}$, $N,N-(\text{C}_{1-10}\text{alkyl})_2\text{amino}$, $\text{C}_{1-10}\text{alkanoylamino}$, $N-(\text{C}_{1-10}\text{alkyl})\text{carbamoyl}$, $\text{C}_{1-10}\text{alkoxycarbonyl}$,

20 $N,N-(\text{C}_{1-10}\text{alkyl})_2\text{carbamoyl}$, $\text{C}_{1-10}\text{alkylS}(\text{O})_a$ wherein a is 0 to 2, $N-(\text{C}_{1-10}\text{alkyl})\text{sulphamoyl}$, $N,N-(\text{C}_{1-10}\text{alkyl})_2\text{sulphamoyl}$, $N-(\text{C}_{1-10}\text{alkyl})\text{sulphamoylamino}$, $N,N-(\text{C}_{1-10}\text{alkyl})_2\text{sulphamoylamino}$, carbocyclyl, carbocyclyl $\text{C}_{1-10}\text{alkyl}$, heterocyclic group, heterocyclyl $\text{C}_{1-10}\text{alkyl}$, carbocyclyl-($\text{C}_{1-10}\text{alkylene}$)_e- R^{43} -($\text{C}_{1-10}\text{alkylene}$)_f- or heterocyclyl-($\text{C}_{1-10}\text{alkylene}$)_g- R^{44} -($\text{C}_{1-10}\text{alkylene}$)_h-; wherein R^{17} may be optionally substituted on carbon by one or more substituents selected from R^{47} ; and wherein if said heterocyclyl contains an $-\text{NH}-$ group, that nitrogen may be optionally substituted by a group selected from R^{48} ; or R^{17} is a group of formula (IC):



(IC)

wherein:

- R^{18} is selected from hydrogen or $\text{C}_{1-4}\text{alkyl}$;
- 5 R^{19} is selected from hydrogen, halo, nitro, cyano, hydroxy, amino, carbamoyl, mercapto, sulphamoyl, $\text{C}_{1-6}\text{alkyl}$, $\text{C}_{2-6}\text{alkenyl}$, $\text{C}_{2-6}\text{alkynyl}$, $\text{C}_{1-6}\text{alkoxy}$, $\text{C}_{1-6}\text{alkanoyl}$, $\text{C}_{1-6}\text{alkanoyloxy}$, $N-(\text{C}_{1-6}\text{alkyl})\text{amino}$, $N,N-(\text{C}_{1-6}\text{alkyl})_2\text{amino}$, $\text{C}_{1-6}\text{alkanoylamino}$, $N-(\text{C}_{1-6}\text{alkyl})\text{carbamoyl}$, $N,N-(\text{C}_{1-6}\text{alkyl})_2\text{carbamoyl}$, $\text{C}_{1-6}\text{alkylS(O)}_a$ wherein a is 0 to 2, $\text{C}_{1-6}\text{alkoxycarbonyl}$, $N-(\text{C}_{1-6}\text{alkyl})\text{sulphamoyl}$, $N,N-(\text{C}_{1-6}\text{alkyl})_2\text{sulphamoyl}$, carbocyclyl or 10 heterocyclic group; where R^{19} may be independently optionally substituted on carbon by one or more substituents selected from R^{51} ; and wherein if said heterocyclyl contains an -NH- group, that nitrogen may be optionally substituted by a group selected from R^{52} ;
- 15 R^{20} is selected from halo, nitro, cyano, hydroxy, amino, carbamoyl, mercapto, sulphamoyl, hydroxyaminocarbonyl, $\text{C}_{1-10}\text{alkyl}$, $\text{C}_{2-10}\text{alkenyl}$, $\text{C}_{2-10}\text{alkynyl}$, $\text{C}_{1-10}\text{alkoxy}$, $\text{C}_{1-10}\text{alkoxycarbonyl}$, $\text{C}_{1-10}\text{alkanoyl}$, $\text{C}_{1-10}\text{alkanoyloxy}$, $N-(\text{C}_{1-10}\text{alkyl})\text{amino}$, $N,N-(\text{C}_{1-10}\text{alkyl})_2\text{amino}$, $N,N,N-(\text{C}_{1-10}\text{alkyl})_3\text{ammonio}$, $\text{C}_{1-10}\text{alkanoylamino}$, $N-(\text{C}_{1-10}\text{alkyl})\text{carbamoyl}$, $N,N-(\text{C}_{1-10}\text{alkyl})_2\text{carbamoyl}$, $\text{C}_{1-10}\text{alkylS(O)}_a$ wherein a is 0 to 2, $\text{N}-(\text{C}_{1-10}\text{alkyl})\text{sulphamoyl}$, $N,N-(\text{C}_{1-10}\text{alkyl})_2\text{sulphamoyl}$, $N-(\text{C}_{1-10}\text{alkyl})\text{sulphamoylamino}$, $N,N-(\text{C}_{1-10}\text{alkyl})_2\text{sulphamoylamino}$, $\text{C}_{1-10}\text{alkoxycarbonylamino}$, carbocyclyl,
- 20 carbocyclyl $\text{C}_{1-10}\text{alkyl}$, heterocyclic group, heterocyclyl $\text{C}_{1-10}\text{alkyl}$, carbocyclyl-($\text{C}_{1-10}\text{alkylene}$) $_e$ - R^{53} -($\text{C}_{1-10}\text{alkylene}$) $_f$ or heterocyclyl-($\text{C}_{1-10}\text{alkylene}$) $_g$ - R^{54} -($\text{C}_{1-10}\text{alkylene}$) $_h$; wherein R^{20} may be independently optionally substituted on carbon by one or more R^{57} ; and wherein if said heterocyclyl contains an -NH- group, that nitrogen may be optionally substituted by a group selected from R^{58} ;
- 25 p is 1-3; wherein the values of R^{15} may be the same or different;
- q is 0-1;
- r is 0-3; wherein the values of R^{16} may be the same or different;
- m is 0-2; wherein the values of R^{12} may be the same or different;
- n is 1-2; wherein the values of R^8 may be the same or different;
- 30 z is 0-3; wherein the values of R^{19} may be the same or different;

R²¹ is selected from hydrogen or C₁₋₆alkyl;

R²² and **R²³** are independently selected from hydrogen, hydroxy, amino, mercapto, C₁₋₆alkyl, C₁₋₆alkoxy, N-(C₁₋₆alkyl)amino, N,N-(C₁₋₆alkyl)₂amino, C₁₋₆alkylS(O)_a wherein a is 0 to 2;

5 **R²⁴** is selected from hydrogen, hydroxy, C₁₋₆alkyl, C₁₋₄alkoxy and C₁₋₆alkanoyloxy;

R²⁵ is selected from halo, nitro, cyano, hydroxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, C₁₋₄alkyl, C₂₋₄alkenyl, C₂₋₄alkynyl, C₁₋₄alkoxy, C₁₋₄alkanoyl, C₁₋₄alkanoyloxy, N-(C₁₋₄alkyl)amino, N,N-(C₁₋₄alkyl)₂amino, C₁₋₄alkanoylamino, N-(C₁₋₄alkyl)carbamoyl, N,N-(C₁₋₄alkyl)₂carbamoyl, C₁₋₄alkylS(O)_a wherein a is 0 to 2, C₁₋₄alkoxycarbonyl,

10 N-(C₁₋₄alkyl)sulphamoyl and N,N-(C₁₋₄alkyl)₂sulphamoyl; wherein R²⁵, may be independently optionally substituted on carbon by one or more R⁶⁷;

R²⁶, R²⁸, R³⁰, R³⁶, R⁴¹, R⁴⁷, R⁵¹ and R⁵⁷ are independently selected from halo, nitro, cyano, hydroxy, amino, carbamoyl, mercapto, sulphamoyl, hydroxyaminocarbonyl, C₁₋₁₀alkyl, C₂₋₁₀alkenyl, C₂₋₁₀alkynyl, C₁₋₁₀alkoxy, C₁₋₁₀alkanoyl, C₁₋₁₀alkanoyloxy, C₁₋₁₀alkoxycarbonyl,

15 N-(C₁₋₁₀alkyl)amino, N,N-(C₁₋₁₀alkyl)₂amino, N,N,N-(C₁₋₁₀alkyl)₃ammonio, C₁₋₁₀alkanoylamino, N-(C₁₋₁₀alkyl)carbamoyl, N,N-(C₁₋₁₀alkyl)₂carbamoyl, C₁₋₁₀alkylS(O)_a wherein a is 0 to 2, N-(C₁₋₁₀alkyl)sulphamoyl, N,N-(C₁₋₁₀alkyl)₂sulphamoyl, N-(C₁₋₁₀alkyl)sulphamoylamino, N,N-(C₁₋₁₀alkyl)₂sulphamoylamino, C₁₋₁₀alkoxycarbonylamino, carbocyclyl, carbocyclylC₁₋₁₀alkyl, heterocyclic group,

20 heterocyclylC₁₋₁₀alkyl, carbocyclyl-(C₁₋₁₀alkylene)_e-R⁵⁹-(C₁₋₁₀alkylene)_f or heterocyclyl-(C₁₋₁₀alkylene)_g-R⁶⁰-(C₁₋₁₀alkylene)_h; wherein R²⁶, R²⁸, R³⁰, R³⁶, R⁴¹, R⁴⁷, R⁵¹ and R⁵⁷ may be independently optionally substituted on carbon by one or more R⁶³; and wherein if said heterocyclyl contains an -NH- group, that nitrogen may be optionally substituted by a group selected from R⁶⁴;

25 **R²⁷, R²⁹, R³¹, R³⁷, R⁴², R⁴⁸, R⁵², R⁵⁸ and R⁶⁴** are independently selected from C₁₋₆alkyl, C₁₋₆alkanoyl, C₁₋₆alkylsulphonyl, sulphamoyl, N-(C₁₋₆alkyl)sulphamoyl, N,N-(C₁₋₆alkyl)₂sulphamoyl, C₁₋₆alkoxycarbonyl, carbamoyl, N-(C₁₋₆alkyl)carbamoyl, N,N-(C₁₋₆alkyl)₂carbamoyl, benzyl, phenethyl, benzoyl, phenylsulphonyl and phenyl;

R³², R³³, R⁴³, R⁴⁴, R⁵³, R⁵⁴, R⁵⁹ and R⁶⁰ are independently selected from -O-, -NR⁶⁵-,

30 -S(O)x-, -NR⁶⁵C(O)NR⁶⁶-, -NR⁶⁵C(S)NR⁶⁶-, -OC(O)N=C-, -NR⁶⁵C(O)- or -C(O)NR⁶⁵-; wherein R⁶⁵ and R⁶⁶ are independently selected from hydrogen or C₁₋₆alkyl, and x is 0-2;

R⁶³ and R⁶⁷ re independently selected from halo, hydroxy, cyano, carbamoyl, ureido, amino, nitro, carbamoyl, mercapto, sulphamoyl, trifluoromethyl, trifluoromethoxy, methyl, ethyl, methoxy, ethoxy, vinyl, allyl, ethynyl, methoxycarbonyl, formyl, acetyl, formamido, acetylamino, acetoxy, methylamino, dimethylamino, N-methylcarbamoyl,

5 N,N-dimethylcarbamoyl, methylthio, methylsulphinyl, mesyl, N-methylsulphamoyl and N,N-dimethylsulphamoyl; and

e, f, g and h are independently selected from 0-2;
or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof.

10 2. A compound of formula (I) according to claim 1 wherein M¹ is -CH₂- and M² is -CR²²R²³-; or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof.

15 3. A compound of formula (I) according to claim 1 wherein M¹ is -CH₂- and M² is -NR²⁴-; or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof.

20 4. A compound of formula (I) according to claim 1 or 2 wherein R²² and R²³ are independently selected from hydrogen and hydroxy; or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof.

25 5. A compound of formula (I) according to claim 1 or 3 wherein R²⁴ is hydrogen; or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof.

6. A compound of formula (I) according to any one of claims 1-5 wherein R¹ and R² are C₁₋₄alkyl; or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof.

7. A compound of formula (I) according to any one of claims 1-6 wherein v is 0; or a 30 pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof.

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WO 2004/076430

PCT/GB2004/000695

- 63 -

8. A compound of formula (I) according to any one of claims 1-7 wherein R⁴ and R⁷ are hydrogen; or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof:

5 9. A compound of formula (I) according to any one of claims 1-8 wherein the R⁵ or R⁶ not selected from a group of formula (IA) is hydrogen or methylthio; or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof.

10. A compound of formula (I) according to any one of claims 1-9 wherein one of R⁵ and 10 R⁶ is a group of formula (IA) (as depicted above); wherein:

Z is -O- or -S(O)_b-; wherein b is 0;

R⁸ is hydrogen;

R⁹ is hydrogen;

R¹⁰ and R¹¹ are independently selected from hydrogen or carbocyclyl; wherein R¹⁰ and 15 R¹¹ may be independently optionally substituted on carbon by one or more substituents selected from R²⁸;

R¹³ is a group of formula (IB) (as depicted above);

R¹⁴ is hydrogen;

R¹⁵ is hydrogen;

20 R¹⁷ is C₁₋₁₀alkyl; wherein R¹⁷ may be optionally substituted on carbon by one or more substituents selected from R⁴⁷; or R¹⁷ is a group of formula (IC) (as depicted above) wherein:

R¹⁸ is selected from hydrogen;

R¹⁹ is selected from hydrogen;

R²⁰ is C₁₋₁₀alkyl; wherein R²⁰ may be independently optionally substituted on carbon 25 by one or more R⁵⁷;

p is 1;

q is 0;

r is 0;

m is 0;

30 n is 1;

z is 1; and

R²⁸, R⁴⁷ and R⁵⁷ are independently selected from halo and hydroxy

or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof.

11. A compound of formula (I) wherein:

M¹ is -CH₂-;

5 M² is -CR²²R²³- and -NR²⁴-;

R²² and R²³ are independently selected from hydrogen and hydroxy;

One of R¹ and R² is ethyl and the other is butyl;

v is 0;

R⁴ and R⁷ are hydrogen;

10 One of R⁵ or R⁶ is selected from a group of formula (IA) (as depicted above) and the other is hydrogen or methylthio;

Z is -O- or -S(O)_b-; wherein b is 0;

R⁸ is hydrogen;

R⁹ is hydrogen;

15 R¹⁰ and R¹¹ are independently selected from hydrogen, 2-fluorophenyl or carbocyclyl;

R¹³ is a group of formula (IB) (as depicted above);

R¹⁴ is hydrogen;

R¹⁵ is hydrogen;

R¹⁷ is pentyl substituted by 5 hydroxy; or R¹⁷ is a group of formula (IC) (as depicted

20 above) wherein:

R¹⁸ is selected from hydrogen;

R¹⁹ is selected from hydrogen;

R²⁰ is pentyl substituted by 5 hydroxy;

p is 1;

25 q is 0;

r is 0;

m is 0;

n is 1; and

z is 1;

30 or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof.

12. A compound of formula (I) selected from:

(+/-)-trans-1,1-dioxo-3-ethyl-3-butyl-5-phenyl-7-methylthio-8-(N-{(R)- α -[N'-(2-(S)-3-(R)-4-(R)-5-(R)-2,3,4,5,6-pentahydroxyhexyl)carbamoyl]benzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,4-benzothiazepine;

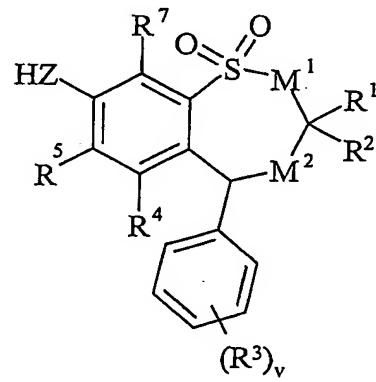
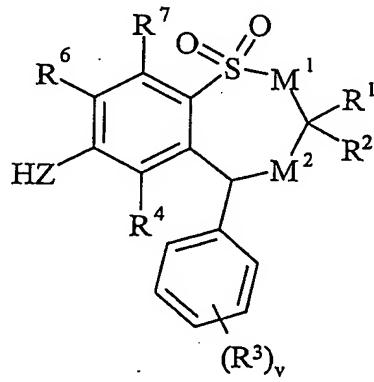
(+/-)-trans-1,1-dioxo-3-ethyl-3-butyl-5-phenyl-7-methylthio-8-(N-{(R)- α -[N'-(2-(S)-3-(R)-4-(R)-5-(R)-2,3,4,5,6-pentahydroxyhexyl)carbamoyl]benzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,4-benzothiazepine;

1,1-dioxo-3-ethyl-3-butyl-4-hydroxy-5-phenyl-7-(N-{ α -[N'-(2-(S)-3-(R)-4-(R)-5-(R)-2,3,4,5,6-pentahydroxyhexyl)carbamoyl]-2-fluorobenzyl}carbamoylmethylthio)-2,3,4,5-tetrahydrobenzothiepine; or

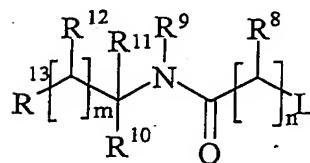
10 1,1-dioxo-3-butyl-3-ethyl-4-hydroxy-5-phenyl-7-(N-{1-[N'-(2-(S)-3-(R)-4-(R)-5-(R)-2,3,4,5,6-pentahydroxyhexyl)carbamoyl]-1-(cyclohexyl)methyl}carbamoylmethylthio)-2,3,4,5-tetrahydrobenzothiepine;
or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof.

15 13. A process for preparing a compound of formula (I) or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, as claimed in anyone of claims 1-12, which process (wherein variable groups are, unless otherwise specified, as defined in claim 1) comprises of:

Process I): for compounds of formula (I) wherein Z is -O-, -NR^a or -S-; reacting a compound
20 of formula (IIa) or (IIb):



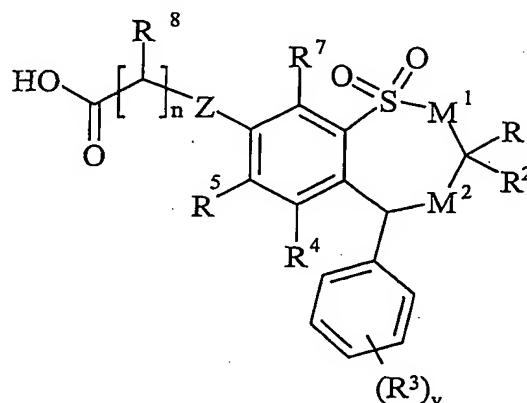
with a compound of formula (III):



(III)

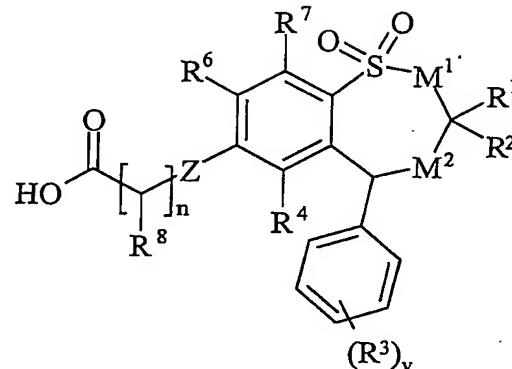
wherein L is a displaceable group;

Process 2): reacting an acid of formula (IVa) or (IVb):



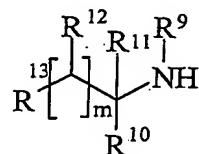
5

(IVa)



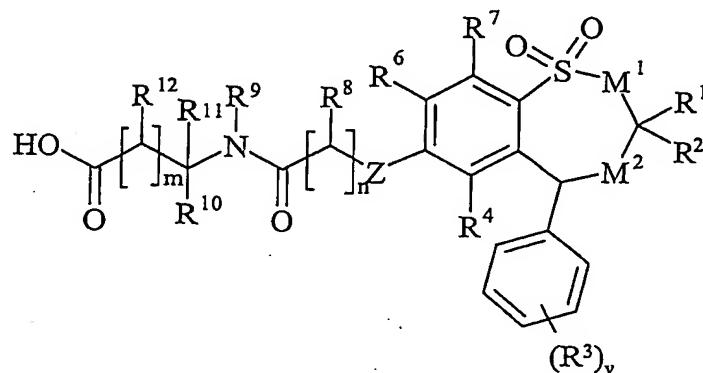
(IVb)

or an activated derivative thereof; with an amine of formula (V):



(V);

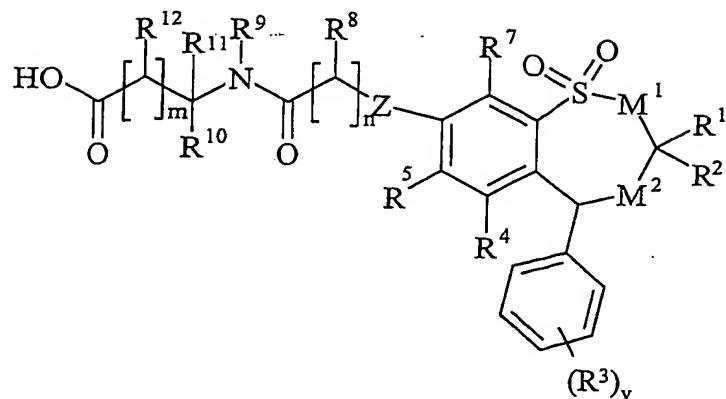
10 *Process 3): for compounds of formula (I) wherein R¹³ is a group of formula (IB); reacting an acid of formula (VIa):*



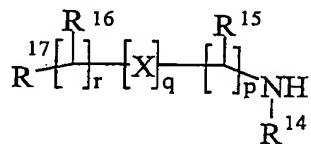
(VIa)

or (VIb):

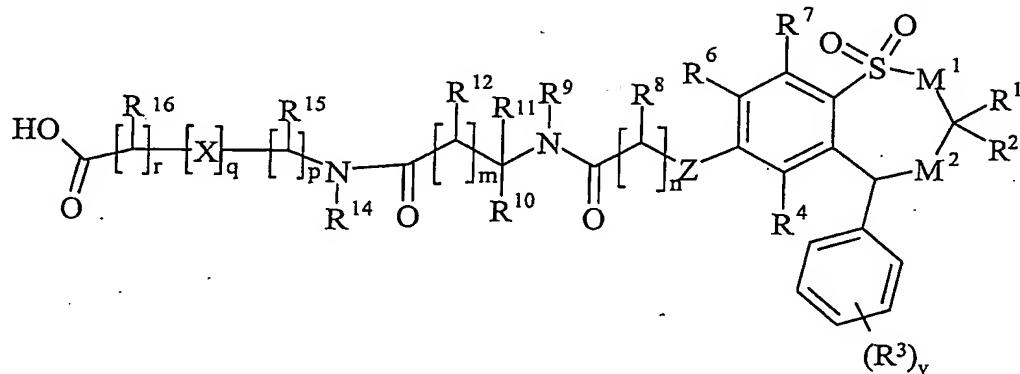
SUBSTITUTE SHEET (RULE 26)



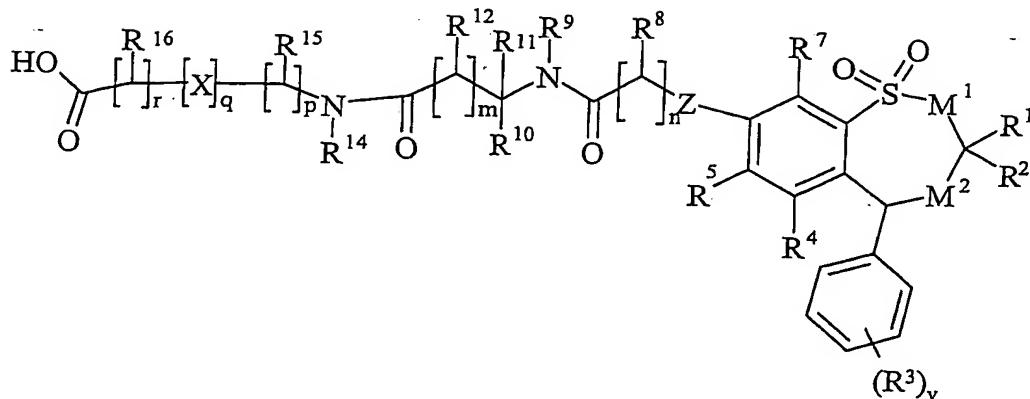
with an amine of formula:



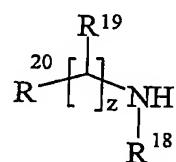
Process 4): for compounds of formula (I) wherein R¹³ is a group of formula (IB) and R¹⁷ is a group of formula (IC); reacting an acid of formula (VIIIa):



10 or (VIIIb)

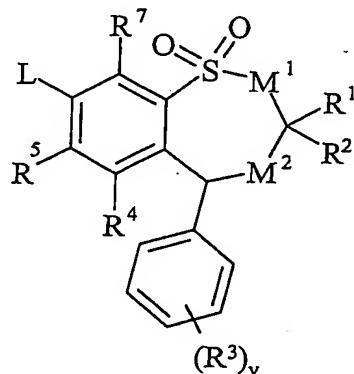
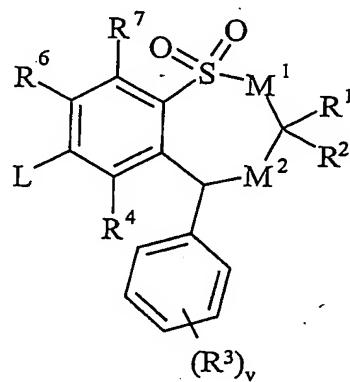


or an activated derivative thereof; with an amine of formula (IX):



5

Process 5) for compounds of formula (I) wherein one of R⁵ and R⁶ are independently selected from C₁₋₆alkylthio optionally substituted on carbon by one or more R²⁵; reacting a compound of formula (Xa) or (Xb):



10

wherein L is a displaceable group; with a thiol of formula (XI):



wherein R^m is C₁₋₆alkylthio optionally substituted on carbon by one or more R²⁵;

15 and thereafter if necessary or desirable:

- i) converting a compound of the formula (I) into another compound of the formula (I);

- ii) removing any protecting groups;
- iii) forming a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug.

14. A compound of the formula (I), or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, as claimed in any one of claims 1 to 12 for use as a medicament.

15. A compound of formula (I), or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, as claimed in any one of claims 1 to 12 for use in a method of prophylactic or therapeutic treatment of a warm-blooded animal, such as man.

16. The use of a compound of the formula (I), or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, as claimed in any one of claims 1 to 12 in the manufacture of a medicament for use in the production of an IBAT inhibitory effect in a warm-blooded animal, such as man.

17. A method for producing an IBAT inhibitory effect in a warm-blooded animal, such as man, in need of such treatment which comprises administering to said animal an effective amount of a compound of formula (I), or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, as claimed in any one of claims 1 to 12.

18. A pharmaceutical composition which comprises a compound of formula (I), or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, as claimed in any one of claims 1 to 12, in association with a pharmaceutically-acceptable diluent or carrier.

19. A combination comprising a compound of formula (I), or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, as claimed in any one of claims 1 to 12, and an HMG Co-A reductase inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof.

20. A combination comprising a compound of formula (I), or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, as claimed in any one of claims 1 to 12, and a bile acid binder.

5 21. A combination comprising a compound of formula (I), or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, as claimed in any one of claims 1 to 12, and an HMG Co-A reductase inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, and a bile acid binder.

10 22. A combination according to claim 19 or claim 21 wherein the HMG Co-A reductase inhibitor is atorvastatin, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof.

23. A combination according to claim 19 or claim 21 wherein the HMG Co-A reductase
15 inhibitor is rosuvastatin, or a pharmaceutically acceptable salt thereof.

24. A combination comprising a compound of formula (I), or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, as claimed in any one of claims 1 to 12 and a PPAR alpha and/or gamma agonist, or a pharmaceutically acceptable salt
20 thereof.

25. A composition according to claim 24 wherein the PPAR alpha and/or gamma agonist is (S)-2-ethoxy-3-[4-(2-{4-methanesulphonyloxyphenyl}ethoxy)phenyl]propanoic acid or a pharmaceutically acceptable salt thereof.